Topic 20: Organic Synthesis

Students will be assessed on their ability to:

20.1	be able to deduce the empirical formulae, molecular formulae and structural formulae from data drawn from combustion analysis, element percentage composition, characteristic reactions of functional groups, infrared spectra, mass spectra and NMR spectra (both ^{13}C and proton)
20.2	understand methods of increasing the length of the carbon chain in a molecule by the use of magnesium to form Grignard reagents and the reactions of the latter with carbon dioxide and with carbonyl compounds in dry ether

Increasing the Carbon Chain Length

1. Introduction of a nitrile group into a compound by reacting a halogenoalkane with KCN (see **10.8v**)
2. Producing hydroxynitriles from carbonyls (see **15.8iii**)
3. Use of Grignard reagents (which is being covered here)

Preparation of Grignard reagents

- A halogenoalkane is dissolved in dry ether and reacted with magnesium to produce the reactive Grignard reagent

$$CH_3CH_2I + Mg \rightarrow \mathbf{CH_3CH_2MgI}$$

Ethyl Magnesium Iodide

- Grignard reagents are highly reactive and the alkyl group (R group) can be considered to have a negative charge, so it can **behave as a nucleophile** $R^-[^+MgI]$
- **Reactions are two steps**
  Reaction of carbonyls and carbon dioxide with Grignard reagent to produce an initial product (in an addition reaction) and then **hydrolysis using dilute acid**

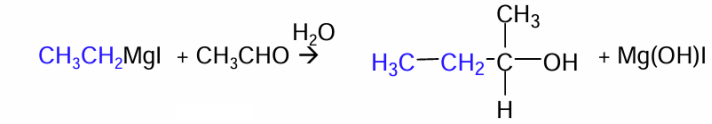
Reaction with carbonyls

1. **With methanal, primary alcohol** is produced

$$HCHO + RMgI \rightarrow RCH_2OH + Mg(OH)I$$

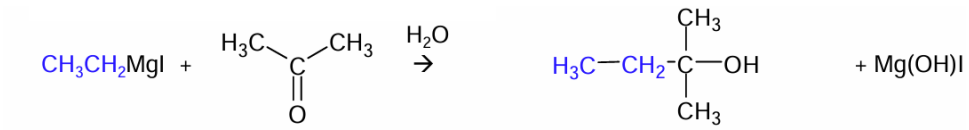
2. **With other aldehydes, secondary alcohol** is produced

$$CH_3CHO + CH_3CH_2MgI \rightarrow CH_3CH_2CH(OH)CH_3 + Mg(OH)I$$



3. **With ketones, tertiary alcohol** is produced

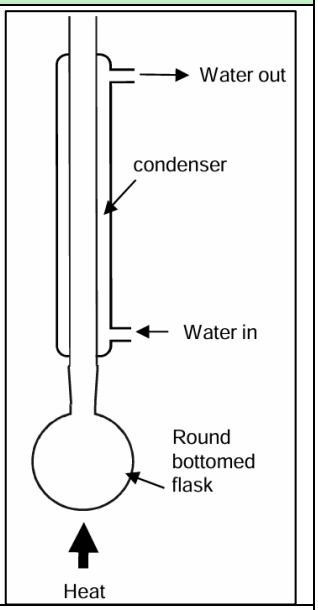
$$CH_3COCH_3 + CH_3CH_2MgI \rightarrow CH_3CH_2C(CH_3)(OH)CH_3 + Mg(OH)I$$



Reaction with carbon dioxide

- **With CO_2, carboxylic acid** is produced

$$CH_3CH_2MgI + CO_2 \rightarrow CH_3CH_2COOH + Mg(OH)I$$

20.3	be able to use knowledge of organic chemistry contained given in this specification to solve problems such as: i predicting the properties of unfamiliar compounds containing one or more of the functional groups included in the specification and explain these predictions ii planning reaction schemes of up to four steps, recalling familiar reactions and using unfamiliar reactions given sufficient information iii selecting suitable practical procedures for carrying out reactions involving compounds with functional groups included in this specification iv identifying appropriate control measures to reduce risk based on data of hazards
20.4	**CORE PRACTICAL 16** **The preparation of aspirin.**
20.5	understand the following techniques used in the preparation and purification of organic compounds: i refluxing ii purification by washing, including with water and sodium carbonate solution iii solvent extraction iv recrystallisation v drying vi distillation vii steam distillation viii melting temperature determination ix boiling temperature determination
i	**Heat under reflux** - Refluxing is used to ensure complete reaction/ oxidation - Heat the reaction mixture at a constant temperature in **a pear-shaped or round bottomed flask** - The condenser prevents organic vapours from escaping by condensing them back to liquids - **Anti-bumping granules** are added to the flask in both reflux and distillation to promote smooth boiling by providing a nucleus for gas bubbles to form on, making small bubbles form instead of large bubbles - The top end of condenser is **never sealed** as the buildup of gas pressure could cause the apparatus to explode - Example reactions: • Production of a carboxylic acid from a primary alcohol using acidified potassium dichromate • Production of an ester from an alcohol and carboxylic acid in the presence of an acid catalyst 
ii	**Purification by Washing** - Washing is used to remove impurities from both a solid and a liquid using water or an organic solvent (or sodium carbonate solution to remove excess acid) - Washing is used when impurities in a sample are soluble in a specific solvent while the desired product is not - Put the impure solid or liquid into a separating funnel - Add a suitable solvent from the following and shake in the separating funnel: 1. **Sodium hydrogencarbonate** solution is used to remove unreacted excess acid (CO_2 gas is produced so pressure needs to be released)

Advantages: Heating at constant temp. prevents side reactions Condenser prevents loss of solvent

Suitable Solvent
The solvent added should be very soluble with the impurities
Desired organic product should NOT be soluble in this new solvent

2. **Water** is used to remove any excess ionic salts
- Then, allow the layers to separate in funnel, and run and discard aqueous layer
- Run the organic layer into a clean, dry conical flask and add three spatula loads of **drying agent** (e.g. anhydrous sodium sulfate, calcium chloride)
- When dry, the organic liquid should appear **clear**
- Carefully decant the liquid into the distillation flask to remove drying agent
- Distill to collect pure product

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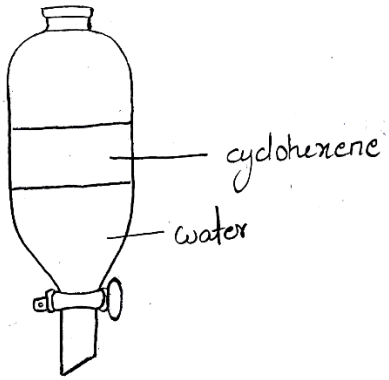
Solvent Extraction
- Mix the mixture to be separated with a suitable solvent in which the desired organic product is more soluble in a separating funnel
- The desired organic compound will then move into the solvent layer where it is most soluble, leaving behind other impurities in the original mixture layer
- The two layers are then separated by running off the layers into separate flasks
- The desired organic compound can then be isolated from the solvent by distillation

Suitable Solvent
The solvent added should be immiscible (does not mix) with the original mixture
Desired organic product should be very soluble in this new solvent



Water is usually produced along with the organic product in reactions
This water will form an aqueous layer while the product will often be in the organic layer
Often, sodium carbonate is also added to neutralize or to remove impurities by washing
A stopper is placed in the neck of funnel and it is inverted and the tap is opened to release pressure (gas)
The funnel is returned to its upright position, the layers are allowed to separate and the aqueous layer is run off

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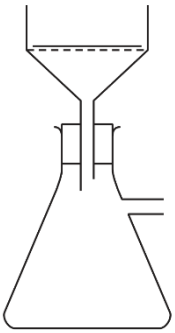
Recrystallisation
- Recrystallisation is used to purify impure solids
- First, dissolve the impure solid in minimum amount of suitable hot solvent to produce a saturated solution (this avoids any loss of desired product)
- Then, filter the hot mixture to remove the insoluble impurities
- After that, allow the solution cool to crystallise/ precipitate the desired solid and this leaves the soluble impurities behind in the solution
- Finally, use suction filtration to remove the soluble impurities and recover the desired crystals
- Wash/ Rinse the crystals with ice-cold solvent to wash off left-over soluble impurities on the crystals (ice-cold is used so that crystals do not dissolve in it)
- Dry the crystals between filter papers or a warm oven (if crystals are not dried properly, mass of yield may appear to be greater than it actually is)
- Example use: in purification of aspirin or azo dyes

Suitable Solvent
Desired solid should be very soluble in it at high temperatures but less soluble at low temperatures

Suction Filtration
Filtration under reduced pressure using Buchner apparatus



This filtration is faster and removes water too (so gives a drier product)

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Drying
- An organic solid can be dried by simply leaving in a warm place or in a desiccator with a drying agent
- An organic liquid will need a suitable drying agent such as anhydrous inorganic salts to remove traces of water from it
- Anhydrous calcium chloride (or magnesium sulfate or calcium sulfate) are mixed with the impure organic product until its appearance changes from cloudy to clear, indicating that it is now dry
- Then the drying agent is separated by filtration or decantation

Don't forget to draw anti-bumping granules in the exam!

Simple Distillation for liquids with a difference in boiling point of more than 25°C

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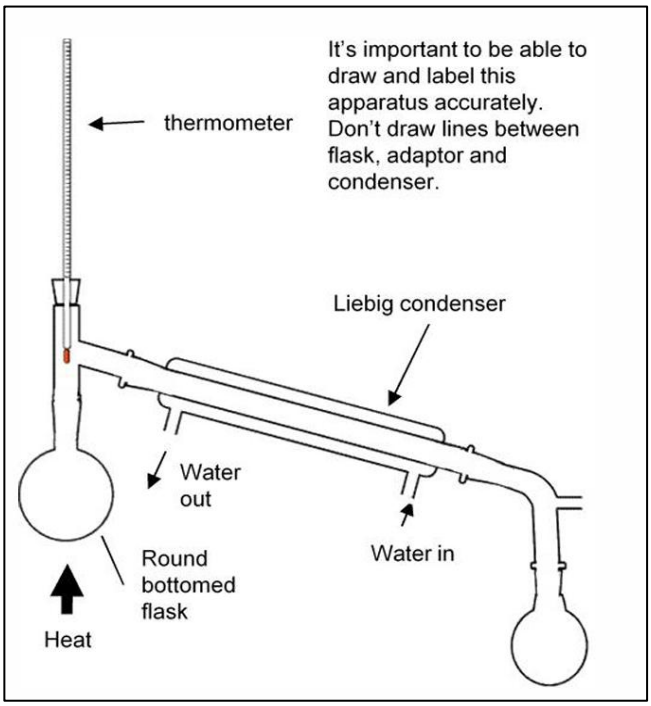
(Simple) Distillation

- In general, it is used to separate an organic product from its reacting mixture based on their boiling points in a **pear-shaped or round bottomed flask**
- Collect the distillate at the approximate boiling temperature range of the desired liquid
- **Anti-bumping granules** are added to promote smooth boiling
- Boiling temperature range between the two liquids must be large
- Example reaction: Production of an aldehyde from a primary alcohol using acidified potassium dichromate solution



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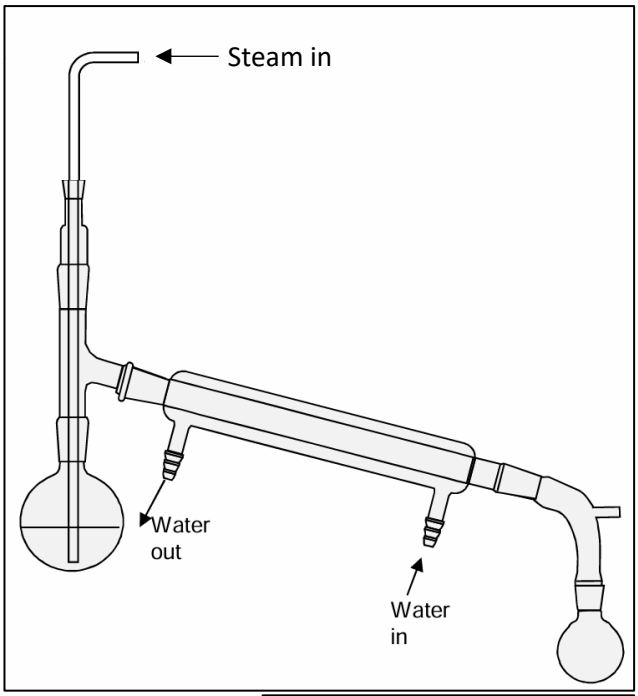
Steam Distillation

- In steam distillation, steam is passed into the mixture and the product vapour is distilled off with the water and condensed
- Steam distillation is used to separate an **insoluble liquid from an aqueous solution**
  - Steam is bubbled into the mixture containing the aqueous solution and the insoluble liquid that forms a separate layer
  - As the steam bubbles through the mixture, it mixes the layers so they form part of the evaporating liquid
  - The resulting distillate can be cloudy if desired compound is not miscible in water
- Advantages are:
  - The insoluble liquid distils at a temperature below its usual boiling point
  - It reduces the chances of thermal decomposition of the insoluble liquid



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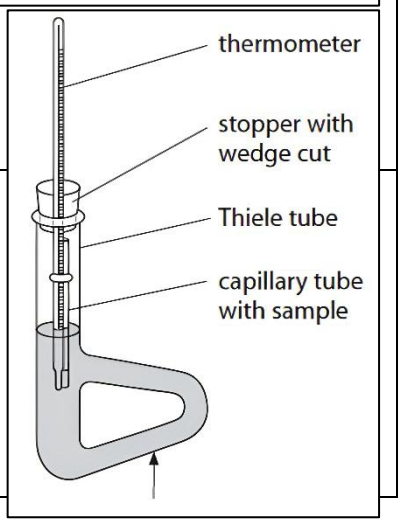
Melting temperature determination

- Melting temperature of a solid is measured using a small capillary tube attached to the bulb of a thermometer and then place the assembly in a liquid that has a boiling temperature above that of the solid
- Then, you can compare it with data book value
- For solids, impurities lower the melting temperature and widen the range at which it melts



ix	**Boiling temperature determination** - For liquids, impurities increase the boiling temperature - You can measure the boiling temperature and compare with data book values - This is a test for purity: if boiling point is sharp, sample is likely to be pure - If there is a range of boiling points, sample contains impurities
	Further suggested practicals: i carry out the preparation of an organic compound, including cholesteryl benzoate (a liquid crystal) or methyl 3-nitrobenzoate ii preparation of oil of wintergreen

Remarks

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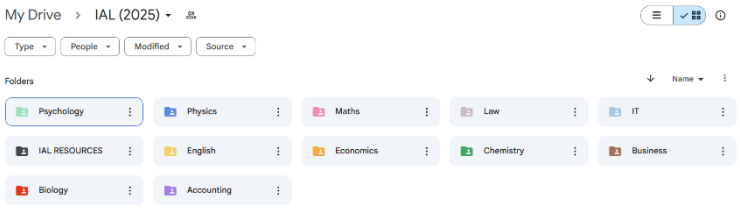

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